

Beliefs and Practices of Nurse Practitioners Related to the Use and Recommendations of
Probiotics for the Prevention of Antibiotic-Associated Vulvovaginal Candidiasis in Adult-aged
Women: An Opportunity for Evidence-based Practice Change.

DNP Final Project

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Abstract

The purpose of this quality improvement project was twofold: (a) conduct semi-structured interviews to explore the beliefs and current practices of Nurse Practitioners (NPs) that prescribe antibiotic therapy in the outpatient setting, regarding probiotic products, and (b) compare these beliefs and practices to the best current evidence. A synthesis of the literature was conducted to describe and critically analyze current best practices of probiotic use in the clinical setting. The results from the semi-structured interviews may augment practice recommendations in clinic settings and effectiveness of probiotics as adjunctive treatment. An executive summary for dissemination to key stakeholders was produced.

The project design included qualitative semi-structured interviews of nine NPs identified using a snowball recruitment method. Responses were recorded on an interview form and common themes to each question were analyzed. Responses were also compared to current evidence-based literature from sixteen peer-reviewed articles that examined the effectiveness of probiotics in the prevention or treatment of certain antibiotic associated side effects.

Although the practitioners' beliefs of symptoms to address with probiotics were generally consistent with current best evidence, gaps in knowledge were identified. The recommendation of probiotic strains and the number of cultures contained in the supplement were discussed in some interviews but was not always in agreement with the literature. Similarly, suggestions regarding the frequency and timing of dosing between the probiotic and the antibiotic recommended by the practitioners were often inconsistent with the research findings.

The main recommendation for the use of probiotics is to suggest probiotics when antibiotics are prescribed to prevent or treat antibiotic-associated diarrhea. For this use, yogurts

containing added live cultures or enteric-coated capsules are most effective. Products should contain 1-10 billion units of probiotic bacteria, be taken three to four times daily, and be continued for two weeks after the antibiotic is complete. Doses of probiotics and antibiotics should be separated by two to four hours to prevent destruction of the probiotic in the GI tract. Probiotics should be avoided in patients with high fevers or immunodeficiency. Current evidence suggests that probiotics are not effective to prevent or treat vulvovaginal candidiasis.

Chapter One: Overview of the Project

Introduction to the Problem

Antibiotics are powerful medications responsible for saving millions of lives and play a pivotal role in medical advancement (Ventola, 2015). Patients frequently seek antibiotics for mild illnesses and viruses such as the common cold; healthcare practitioners often prescribe them to appease patient requests (Ventola, 2015). Unfortunately, this practice is a misuse of antibiotics resulting in the over prescription of antibiotics which has blunted their impact in the treatment of bacterial infections (Ventola, 2015). According to the Centers for Disease Control and Prevention (CDC), in 2104, 266 million courses of antibiotics were dispensed in the United States (CDC, 2016). That equates to one antibiotic prescription each for 83 percent of the population annually.

A problem associated with antibiotic treatment is that the antibiotics not only kill bacteria associated with infection, but also inhibits the body's natural bacterial flora creating an environment favoring potential pathogens such as candida (Sobel, 2015). When the balance of good bacteria is disrupted, a condition called dysbiosis (e.g., microbial imbalance) occurs, potentiating a wide range of possible side effects including diarrhea, stomach upset, overgrowth of resistant bacteria such as *Clostridium difficile* (C. diff), and fungal over-growth (Rodgers, Kirley, & Mounsey, 2013). Fungal over-growth leads to oral thrush, skin infections, and vulvovaginal candidiasis (VVC) commonly known as vaginal yeast infection (Gillies, Ranakusuma, Hoffmann, Thorning, McGuire, Glasziou, & Del Mar, 2015).

Uncomfortable symptoms associated with antibiotic-associated side effects such as VVC are a main reason for patient treatment non-compliance and discontinuance of antibiotic therapy (Rodgers, et.al.). The World Health Organization (2015) recognizes incomplete antibiotic

treatment as a key contributor in the creation of antimicrobial-resistant organisms and as a serious hazard to global public health threatening effective prevention and treatment of infections caused by bacteria, viruses, parasites, and fungi. Increasing medication compliance as well as reducing the need for antifungal medications can help to prevent antimicrobial resistance.

Women of child-bearing age are particularly susceptible to antibiotic-associated VVC. According to Sobel, one quarter to one third of women experience VVC after taking a broad-spectrum antibiotic (2015). Women prone to VVC often request prescriptions for Diflucan, an antifungal medication, at the time an antibiotic is prescribed. Women often self-manage the fungal infection with probiotics (Pirota & Garland, 2005) or with prescribed Diflucan. A recent study revealed that as few as 11% of women correctly self-diagnose VVC infections following antibiotic use, although the number of cases of correctly self-diagnosed VVC could be as high as 35% in women who had been professionally diagnosed previously with VVC (Sobel, 2015). The over prescription of antifungal treatment such as Diflucan is a healthcare provider issue contributing to microbial resistance (WHO, 2015), and is associated with drug resistant strains of *Candida* (Hu, Merenstein, Wang, Hamilton, Blackmon, Chen, & Li, 2013). VVC can be caused by antibiotic use and is a common reason for early discountenance of antibiotic treatment (Sobel, 2015).

Medication compliance is essential for effective management of disease. The side effects of gastrointestinal upset and VVC are frequent causes of antibiotic noncompliance. Evidence-based identification of correct indications, doses, strains of probiotic organisms, and patient education of probiotics may help to reduce side effects and improve compliance (Pirota & Garland, 2005). Understanding these factors enables practitioners to safely recommend

probiotics that have strong evidence benefitting patients and the preservation of future antibiotic effectiveness.

Significance to Nursing

The issues of minimizing side effects and maximizing antibiotic compliance are relevant to nursing and to effective healthcare delivery overall, as Nurse Practitioners (NPs) have become major providers of care and advocates for patients in the primary care environment. The CDC (2016) reports that 80-90% of antibiotic prescriptions are written in the outpatient setting. According to the American Association of Nurse Practitioners (2016), 83% of NPs work in primary care; those working full time write an average of 23 prescriptions each day including antibiotic prescriptions. As prescribers of antibiotics, NPs must prescribe based on the best and current evidence as well as guidelines for care to ensure improved medication compliance, proper patient education, and better patient outcomes.

In the primary healthcare environment, head, eye, ear, nose & throat (HEENT) infections such as streptococcal pharyngitis (Chow & Doron, 2013), acute otitis media, and sinusitis are common reasons that patients seek care that result in antibiotic treatment (American Academy of Otolaryngology, 2016). First-line treatments for these infections are penicillin-based antibiotics such as Amoxicillin, Augmentin, and Phenoxymethylpenicillin (PenVK) that require a seven to ten day course of care (American Academy of Otolaryngology, 2016). These medications are known to cause VVC for as many as 33% of women taking antibiotics for non-urogenital purposes (Sobel, 2015) contributing to antibiotic non-compliance and use of antifungal treatments such as Diflucan.

It is estimated that more than 30% of people who take antibiotics will experience some degree of adverse effects associated with the disruption of flora (McFarland, 2015). Recently, it

has become more common for healthcare providers prescribing antibiotics to recommend taking a probiotic when ordering an antibiotic for a patient (Rodgers, et al., 2013). According to McFarland (2015) patients depend on healthcare providers for information on probiotics, but instead many patients receive information on probiotics from web-based sources found on the Internet. Credibility of effectiveness claims regarding probiotics contrast greatly from Pirotta & Garland (2005) claiming decades of acceptance of probiotics as a “folk remedy” for VVC prevention to 98% of gastroenterologists expressing belief in probiotics for flora imbalance treatment including some yeast infections and gastrointestinal symptoms (Rodgers, et al., 2013). To properly advise patients, NPs need to be guided by evidence-based practice in order to make recommendations that will benefit patients and lead to better health outcomes.

Antibiotic resistance is a concern to nursing, healthcare, and public health. In 2016, “superbugs” resistant to all known antibiotics have surfaced, resulting in increased patient mortality (Chen, Todd, Kiehlbauch, Walters, & Kallen, 2017). To address antibiotic use, the White House National Action Plan for Combatting Antibiotic-Resistant Bacteria (2015) was formed to reduce inappropriate outpatient antibiotic use by 50 percent by the year 2020, including reducing antibiotics prescribed for otitis media by 50%. As antibiotic non-compliance has been identified as a primary contributor in microbial resistance, nurse leaders such as Doctor of Nursing Practice prepared nurses must work to improve evidenced-based practice by creating and implementing guidelines and protocols based on current best evidence. This standardization of practice will reduce non-compliance and prevent microbial resistance.

Purpose

The purpose of the quality improvement project was twofold: (a) to conduct semi-structured interviews to explore the beliefs and current practices of nurse practitioners that

prescribe antibiotic therapy regarding probiotic products, and (b) compare these beliefs and practices to the best current evidence. A synthesis of the literature was conducted to describe and analyze best practices of uses for probiotics in the clinical setting. The results from the semi-structured interviews may identify a need for practice change or augment practice recommendations for the use of probiotics as adjunctive treatment. An executive summary for dissemination to key stakeholders was produced (see Appendix F).

Clinical Practice Problem Statement

Among nurse practitioners prescribing antibiotics for adult age women with HEENT infections, how do their beliefs and practices regarding probiotic use compare with evidence-based practice recommendations to prevent vulvovaginal candidiasis?

Chapter Two: Review of Literature

Many clinical indications for probiotics have been studied in the literature including bacterial vaginitis (McFarland et.al, 2015; Abad & Safdar, 2009), VVC (Abad & Safdar, Hu, et.al, 2013, Gillies, et.al, 2015), oral thrush (McFarland, et.al, 2015, Hu, et.al 2013), antibiotic-associated diarrhea (Avadhani & Steefel, 2015; McFarland et.al, 2015; World Gastroenterology, 2011), and C.Diff infections (McFarland et.al, 2015; World Gastroenterology, 2011). Although initial searches focused mainly on probiotic use associated with VVC, stronger evidence was identified for clinical uses of probiotics associated with gastrointestinal disturbances during antibiotic therapy (Avadhani & Steefel, 2015; McFarland et.al, 2015; World Gastroenterology, 2011). Additional studies acknowledged the usefulness of probiotics in treating oral thrush, skin infections, and overall immune health (McFarland, et.al, 2015). No studies were located that addressed nurse practitioners recommending probiotic use for any purpose.

Literature Review

The project design is conceptually guided by a quality improvement framework that began with a systematic literature search on the topic using inclusion and exclusion criteria, collection and analysis of the level-of-evidence, and recommendations in relation to the existing published research and practice guidelines. The resulting data were compiled into a literature synthesis table (see Appendix A) and evaluated for level and quality of evidence. Specifically, the project followed the *Six Sigma* methodology. *Six Sigma* is a problem-solving method using the five-step DMAIC Process for quality improvement (Moran, 2012). The steps of the DMAIC process are: Define measure, analyze, improve, and control. The purpose of quality improvement drives this design because this project focuses on the improvement of a practice-based concern.

The evidence used to develop this quality improvement project resulted from a systematic review of the literature focused on peer-reviewed, published research on probiotic use with antibiotics. Inclusion criteria included studies: (a) focused on treatment of antibiotic-induced yeast infections, (b) comparing probiotic use in combination with an antibiotic to antibiotic use alone, (c) examining yeast infections and probiotics, (d) including women between the ages of 21 and 45 years old, and (e) studies that address administration frequency, timing, and dosing of probiotics for adjunct clinical use with antibiotic therapies. Exclusion criteria included oral yeast infections such as thrush, skin infections, men, children, and women younger than 21 or older than 45 years of age.

First, online database literature searches were performed through the Health Sciences Library at Ohio State University using the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Medical Literature Analysis and Retrieval System Online (MEDLINE) databases. The search/MESH terms employed included: antibiotic, probiotic, lactobacillus, yeast, candidiasis, fungal, vaginal, vaginitis, vulvovaginal, prevention, prophylactic, treatment, and female. Initial results identified 78 articles, of which 34 were selected for review (9 duplicates were removed, and 25 articles met exclusionary criteria). Sixteen papers were determined to be relative to this project and are included in this review and in the synthesis table (see Appendix A). Of the 16 included papers: three were systematic reviews, four were randomized control trials, four were pilot or mixed method studies, and five were expert opinions.

Next, the papers identified were analyzed for strengths and limitations using the Rating System for the Hierarchy of Evidence (Melnik, 2011) in which study designs are rated for reliability and minimizing bias. Using this scale, levels of evidence were applied using the Center for Transdisciplinary Evidence Based Practice Rapid Critical Appraisal Tool (Melnik,

2011). The appraisal process was used to identify best practices for clinical decision-making, therefore the data must be of the highest statistical worth on which to base clinical change (Moran, Burson, & Conrad, 2014). Level I evidence, that with the highest worth included systematic reviews by Abad & Safdar (2009) and Hanson, VandeVusse, Jerme, Abad, & Safdar, (2016). Level II evidence includes randomized controlled studies (RCTs) such as Bohbot & Cardot (2012), Hu, et al. (2013), Pendharkar, Brandsborg, Hammarstrom, Marcotte, & Larsson, (2015), Chew & Than (2016), Pirotta, Gunn, Chondros, Grover, O'Malley, Hurley, & Garland, (2004), Tomusiak, Strus, Heczko, Adamski, Stefański, Mikołajczyk-Cichońska, & Suda-Szczurek, (2015). Level III evidence includes controlled studies such as Vicariotto, Del Piano, Mogna, & Mogna, (2012). Level VII evidence includes expert opinion articles such as McFarland (2015), Neafsey (2005), Pirotta & Garland (2005), Reid & Bruce (2003), Grazul, Kanda, & Gondek (2015).

While the evidence from the peer reviewed research overall was not found to be statistically significant in support of probiotics for VVC, preventatively or curatively, several studies did note encouraging findings that warranted further research. For example, Vicariotto, et al., (2012) stated, “probiotics are emerging as a new strategy to counteract VVC” (pg. 73), noting that probiotics helped establish a natural barrier to some yeasts by decreasing intervaginal pH. They also found that by using slow release vaginal probiotic tablets a decrease in recurrent VVC, not associated with antibiotic use was noteworthy. Similarly, Hanson et al., (2016) state “it is plausible that more investigation would have had significant findings if antibiotic and probiotic interventions were more carefully timed and clearly reported” (pg. 353). Pirotta, et al., (2004) note that most trials to date have been methodically poor, lacking adequate concealment, randomization, or control. Although at this time evidence is weak to support clinical use of

probiotics for VVC, future studies may identify the specific strains, doses, and routes of administration to be clinically significant.

Bobhot & Cardot (2012) suggest that great variability in clinical results is due to the number of variables being studied. Too many variables with small samples can lead to non-significant findings even when one exists. Bobhot & Cardot recommend that the variation in probiotic preparations, routes of administration, and duration of treatments require rigorous clinical trials to further investigate dosing and vaginal uptake (2012). Pendharkar, Brandsborg, Hammarstrom, Marcotte, & Larsson (2015) further suggest that for child-bearing age women menstrual cycle stage as a factor important to vaginal uptake of probiotics for VVC prevention and treatment is not well understood but should be considered for studies. Further, Tomusiak et al., (2015) identified three *Lactobacillus* strains most effective in vaginal uptake and the effect on vaginal pH, a measure thought to be key in the development of VVC. Their study combined the three strains into a single intravaginal product found to be effective in a placebo-controlled trial. These studies indicate that more robust research is being done to identify strains and doses of *Lactobacillus* effective in restoring vaginal microbiota to prevent or treat VVC. This promising research may lead to better evidence to guide practice.

Some researchers discussed concern for the ability of probiotics to survive the GI tract in order to exert their effectiveness. McFarland (2015) noted the importance of using strains resistant to gastric and bile acidity, while Hanson, et al., (2016) advocate separating antibiotic and probiotic doses by at least two hours declaring that the antibiotic could destroy the probiotic in the GI tract. Enteric-coated probiotic capsules protect the cultures from stomach acid, allowing absorption in the small intestine (Bobhot & Cardot, 2012).

Several authors specified lactobacillus, which Neafsey & Donat (2005) described as having a greater ability to transfer and colonize vaginally. Bobhot & Cardot (2012) state that Lactobacillus is fundamental for eco balance of the vagina. Reid & Bruce distinguish Lactobacillus rhamnosus and Lactobacillus fermentium as having some activity in the inhibition of Candida yeasts (2003). Many strains and combinations were studied; lactobacillus and acidophilus (Vicariotto, et al., 2012), Lactobacillus casei rhamnosus (Bobhot & Cardot, 2012), and Lactobacillus rhamnosis, Lactobacillus gasseri (Pendharker, et al., 2015). A study by Tomusiak, et al, (2015) successfully used a probiotic product that contained three strains of Lactobacillus in a study compared to placebo.

Yogurt is a common probiotic, but it is important to know that not every yogurt is a probiotic (McFarland, et al., 2015). Mixed results were found using yogurt as a probiotic, with positive results reported using yogurt with added live or active probiotic cultures (Hu, H., et al., 2013). Pirotta & Garland (2005) felt that yogurt was too unstable to be seriously considered due to shelf life and low standards of quality control; further noting that yogurt is held to food standards, not pharmaceutical standards and depended instead on isolated probiotics for both oral and vaginal administration.

With limited statistical findings, researchers agree that probiotics may have some promise in the prevention of antibiotic associated VVC; all studies concluded that more research is needed. Probiotics are considered to be complementary/alternative medicines (CAM) and therefore do not have the monetary research funding priority compared to pharmaceutical studies (Pirotta, et al., 2004). Despite probiotics being a \$48 billion dollar a year industry, only six percent of probiotic research focuses on vaginitis, and only a fraction of that specifically studies VVC (McFarland, 2015). Up to 30% of women experience antibiotic-induced VVC when using

broad-spectrum antibiotics, a problem that affects medication compliance. If researchers have found encouraging results, research should continue to advance clinical practice and improve patient outcomes.

It is important to note that though probiotics as prophylaxis or treatment for VVC is still being investigated, their use as adjunct therapy to antibiotics is well documented for antibiotic-induced gastrointestinal symptoms. Probiotic use as a preventative measure for antibiotic associated diarrhea and *C. diff* is well documented in the World Gastroenterology Organization Global Guidelines (2011), and studies conducted by Pattani, Palda, Hwang, & Shah (2013). No studies have determined probiotic use or supplementation with probiotics to be harmful in any way.

Gaps in Evidence

An exhaustive literature review reveals that the evidence to support the pairing of probiotics with antibiotics to prevent VVC is weak though research continues attempting to identify strains and preparations of probiotics effective for VVC. Further research is needed to better understand the pathogenesis and treatment of post-antibiotic VVC. These gaps highlight opportunities for future research to improve clinical practice.

Quality of probiotics is cited as a concern (Abad & Safdar, 2009). Probiotics are considered to be dietary supplements and are not regulated by the United States Food and Drug Administration (FDA), so manufacturing techniques, claims of effectiveness, or actual contents of the supplement are not assured (National Institute of Health, 2015). Studies by Vicariotto et al., (2012), Tomusiak, et al., (2015), Abad & Safdar, (2009) identify timing, dosing, and optimal administration routes as areas needing further clarification in research. Hanson, et al., (2016) say more measurable purposes and outcomes need to be explored. Six percent of probiotic research

focuses on vaginitis, and a fraction of that specifically studies VVC (McFarland, 2015).

Allocating better funding will enable researchers to perform more and better research to identify strains, doses and routes with better efficacy.

The literature search yielded no findings related to nurse practitioner or healthcare provider practices regarding probiotic recommendation and patient education. Addressing these gaps can help to ensure that nurse practitioners are practicing using current evidence, and teaching patients safely and effectively how to care for their own health.

Theoretical Framework

The theoretical framework utilized for the development of this project is *Promoting Action on Research Implementation in Health Services* (PARIHS) as defined by Kitson, Harvey, & McCormack (1998). This framework is useful as a guide to implement evidence-based practice into the clinical practice setting. The three key factors of PARIHS include: Evidence, Context, and Facilitation (Kitson, Harvey, & McCormack, 1998).

Evidence. Evidence refers to not only the literature and research that is to be translated into practice, but includes practitioner expertise and experience, the intended population to be affected, and the context or environment (Kitson, et al., 1998). These factors fit well with this project in comparing the best evidence to nurse practitioner perceptions and beliefs. These findings can be translated into clinical practice for applicable patients.

Context. Context encompasses the culture, environment, and implementation strategies of change to be applied (Kitson, et al., 1998). In the case of this quality improvement project, this aspect takes factors such as patients at risk and individual factors such as the antibiotic to be prescribed into consideration for the treatment plan. The interview questions were designed to provide insight to the thoughts, experiences, patient teaching or education, and recommendations

of the nurse practitioners when prescribing antibiotics. The results were compared with the current best evidence defined by the comprehensive review of the literature to identify best practice.

Facilitation. Facilitation is a process to include the practitioner's existing knowledge and skill in applying the new information (Kitson, et al., 1998). It may also be interpreted as enabling or empowering the practitioner in a mentoring or supportive manner. It is a knowledge translation strategy that may be utilized as dissemination of evidence in this project. An executive summary was created detailing findings and identifying best practices revealed in the project. This summary will be made available for dissemination to nurse practitioner journals where nurse practitioners can update their own knowledge and practices, improving care for their patients.

Chapter Three: Methodology

Project Design and Methodology

Evidence-based practice is the action of making clinical decisions based on the best current available evidence to ensure that changes to nursing practice and patient care are grounded in the highest quality research at the given time. In this quality improvement project, this means using the best current evidence to drive probiotic use in the clinical setting. The best available evidence refers to rating research on the Hierarchy of Evidence scale, recognizing that the highest levels of research are valid, reliable, and applicable while minimizing bias (Melnik & Fineout-Overholt, 2015). This data must be combined with practitioner expertise and clinical experience as well as the needs of the patient or population while fitting with the mission of the organization to identify and provide the highest quality of safety and care for patients.

The Iowa Model

The Iowa model is an evidence-based practice framework that can be applied to a clinical innovation ensuring a process of implementation that addresses the intricacies of change (Melnik & Fineout-Overholt, 2015). The Iowa model was used in the implementation of this project using the following steps:

Assess the need for change. The nurse practitioners interviewed are prescribing professionals who see patients for “sick” visits, many of these episodic visits result in a prescription for antibiotics. During the nurse practitioner and patient discussion, education on expectations of treatment, including side effects often takes place. The topic of probiotics may be discussed at that time. This quality improvement project utilized a semi-structured tool to interview nurse practitioners, revealing their beliefs and practices regarding probiotic

recommendations (See Appendix D). The interview tool incorporated views of key stakeholders, current practice(s), and relevance of health problems to outcomes.

Locate the best evidence. The evidence detailed in the literature review was used to identify the scientific basis for clinical probiotic use. Further information to guide the practice was obtained in the semi-structured interviews to assess current probiotic practices and beliefs in the patient care setting.

Critically analyze the evidence. The evidence identified in the literature review concluded that evidence does not support the practice of using probiotics in the prevention or treatment of antibiotic-induced VVC, however stronger evidence does exist to use probiotics for many gastrointestinal side effects including gastritis and antibiotic-induced diarrhea. The evidence shows when probiotics are indicated and when they should be taken for maximum effect. For example, probiotics are indicated for use when taking a broad-spectrum antibiotic likely to cause gastrointestinal symptoms, and should be taken three to four times a day during the antibiotic course, and for two weeks after antibiotic completion (Avadhani & Steefel, 2015; McFarland et.al, 2015).

Design a practice change. The best evidence indicates that a current practice should discontinue any recommendation of probiotic use for VVC, but include probiotics to prevent gastrointestinal symptoms when broad-spectrum antibiotics are prescribed, in accordance with the recommendations as detailed in the practice change section of this paper. Using the best current peer-reviewed literature and the results from nurse practitioner interviews, an Executive Summary for dissemination to key stakeholders was produced. The Executive Summary highlighted key points: when probiotics are and are not effective in clinical use and the best ways to incorporate their use into the treatment plan.

Implement and evaluate the change in practice. The Executive Summary was made available to stakeholders to disseminate results to guide clinical conversations with patients in the expectation, prevention and treatment of antibiotic-associated VVC and other clinical uses for probiotics.

Integrate and maintain the change. The results of the project will be submitted for publication to a peer-reviewed nurse practitioner periodical. Results will be further disseminated through professional conference presentations.

Project Design

This quality improvement project used a qualitative approach, guided by a critical analysis of the literature. Six, semi-structured, open-ended interview questions were crafted to encourage the nurse practitioner participants to openly discuss their perceptions, beliefs, probiotic knowledge, and probiotic patient care practices in regard to clinical use.

The project was a quality improvement endeavor to compare practitioner beliefs and perspectives combined with a critical appraisal of the current evidence to determine if practices regarding probiotics are grounded in the best scientific evidence. No personal or identifiable health information was gathered for this project, and no patient data was utilized. Quality improvement projects are not subject to Institutional Review Board (IRB) approval, thus based on these factors; this project was determined to be exempt from IRB approval by the Ohio State University (see Appendix B). The quality improvement versus research assessment interactive tool was used and the verification IRB form will serve as documentation of meeting criteria for exemption from IRB review.

Sample

The sample included nine nurse practitioners currently practicing in the state of Ohio with prescriptive authority to prescribe antibiotics. Participants were employed in a prescribing patient care role in an ambulatory or primary care clinic that agreed to participate in the project.

Participants were identified using the snowball method of recruitment. With snowball recruitment, each participant was asked to recommend 2-3 other nurse practitioners for possible inclusion. By using snowball methods, the sample would be more diverse and representative of the nurse practitioner population in the geographical region. In this snowball or referral-based recruitment method, initial participants were offered information sheets to voluntarily share with colleagues who may be appropriate for the project (Boise State University, 2016). Potential participants willing to be interviewed made the initial contact with the interviewer, at which time an in-person; private interview was arranged at a time and location at the convenience of the participant. The initial contact with one NP known to the interviewer agreed to be interviewed and to refer peers not known to the interviewer. The process was slow and several potential subjects did not contact the interviewer. A second contact known to the interviewer was reached and also agreed to be interviewed and help recruit subjects. The overall response rate was 47%; nineteen invitations were extended with nine subjects completing the interview. The response was adequate to reach saturation wherein common themes were emerging without generating new findings.

Data Collection Process

The methods of this project entailed several steps. First, the DNP student interviewer prepared a disclosure and consent document (see Appendix C) explaining the purpose, procedure, and objectives of the project. After reading the document, nine participants elected to

continue and participated in an interview lasting approximately ten minutes. Second, the interviewer took handwritten notes on the interview form (see Appendix D), and third, the interview was recorded without including identifying information about the participant. The recording was destroyed after it was transcribed and notes were confirmed to be accurate.

The interview consisted of six questions, plus follow up questions as appropriate. Optional demographic information was collected. Although the questions were structured to avoid risks, participants were free to decline any question, and to withdraw from the interview altogether at any time, however no participants chose to withdraw. Following the interview, the fourth step was to offer participants copies of an “Invitation to Participate” (see Appendix E) that they could voluntarily share with peers who may be willing to participate in the project. It was expected that 6-12 interviews would be necessary to reach saturation. Saturation is defined as the point at which the same responses or themes are emerging without new information being obtained. For this project, saturation of findings was obtained after nine interviews were completed.

Chapter Four: Findings

Sample Characteristics

Nine nurse practitioner (NP) participants completed interviews over a one-month period. The nurse practitioners ranged in experience, from two years of practice, to 22 years in practice with 33% (n = 3) having more than 15 years of experience, and 44% (n = 4) having less than five years of experience. Seven of the nine nurse practitioners were certified as Family Nurse Practitioners (FNP), one was certified as an Adult Nurse Practitioner (ANP), and one was a certified Pediatric Nurse Practitioner (PNP). The sample consisted of mostly females, 88% (n = 8) with only one male participant. All nurse practitioners prescribed antibiotics, with practice settings to include primary care, retail health, urgent care, and pediatrics. Two of the NPs were working in specialty settings at this time. All participants stated that they had no instruction regarding probiotics in their NP education and shared that their information regarding probiotics came from advertising, 33% (n = 3) and from professional journal articles, 77% (n = 7) while 33% (n = 3) also reportedly gained information from colleagues.

Survey Questions and Responses

Question 1: What are your thoughts and experiences regarding the clinical recommendation of probiotics for patients?

All NPs interviewed expressed their perceived effectiveness of probiotics in managing GI symptoms such as diarrhea, while 55% (n = 5) discussed the importance of maintaining balance of natural flora. Specific patient scenarios were identified by 55% (n = 5) of the interviewees in their decision to recommend probiotics, noting that probiotics were useful in cases following colonoscopy, after viral illness, during periods of GI upset or heartburn, and with antibiotic use. Several interviewees noted that populations most likely to be receptive to probiotics were women

ranging in age from about age 40 to 60 years old, and those with a higher health IQ. Three NPs noted a lower level of receptiveness in patients of a lower socioeconomic status, which they speculated as being due to some combination of health literacy and being able to afford the additional products which might not be covered by insurance.

Question 2: Do you prescribe antibiotics? If so, what is your experience with the efficacy of probiotics to prevent or treat antibiotic-associated side effects?

All nine nurse practitioners interviewed had experience prescribing antibiotics. Specific antibiotics likely to cause side effects were identified by more than half of the interviewees (55%). Three nurse practitioners said Augmentin caused side effects; Macrolide antibiotics such as Azithromycin were noted by two NPs as causing side effects; and broad-spectrum antibiotics were stated by two NPs without naming a specific drug. One NP noted conditions needing higher doses of antibiotics as likely to increase side effect symptoms, and another NP mentioned cases where a second round of antibiotics was necessary. In five interviews (55%), nurse practitioners said that they do find probiotics to be helpful to address side effect symptoms.

2a: Which side-effect symptoms are you concerned about?

All nine practitioners listed diarrhea or loose stools first as a symptom of concern. Gastrointestinal symptoms including heartburn, GI upset, and gastritis were identified by 44% (n = 4) of respondents. Yeast overgrowth was voiced as a concern in 44% (n = 4) of the responses noting specifically skin and oral thrush. Only 22% (n = 2) of NPs mentioned VVC, and one NP identified balanitis as a potential concern (interestingly, two NPs specifically noted diabetes as a risk factor related to yeast overgrowth secondary to antibiotic use). Three (33%) nurse practitioners pointed out the preventative use of probiotics so that symptoms do not develop.

Question 3: If you recommend probiotics to patients, how do you recommend they be taken?

The most common response (44%) to recommending how to take probiotics was to follow the directions on the package (n = 4). One nurse practitioner stated that if package directions state one a day, but they are taking antibiotics, taking 2 or 3 each day of probiotic treatment would be recommended. Although 44% (n = 4) NPs spoke of the following package directions, more than half or 55% (n = 5) referred to yogurt when discussing probiotics. Of these, two NPs stated “live active cultures”, one NP stated “Activa” – a name brand. Three interviewees voiced concern for sugar in yogurt and diabetes was stressed as a reason for concern. Only one interviewee recommended patients take the probiotic prior to antibiotic use.

Interestingly, only one NP specifically stated that probiotics would **not** be recommended to patients. This practitioner did not cite ineffectiveness as the reason, but that probiotics are an added expense and patients in the free clinic setting cannot afford them. This NP also cited lower health literacy for patients and stated “most patients just want the antibiotic and be done with it”.

Question 4: Do patients ask about probiotic use when you prescribe antibiotics?

Describe or explain how you respond.

All nine nurse practitioners stated that patients seldom ask about probiotics. Most NPs, 66% (n = 6) replied that when probiotics are discussed it is most often the nurse practitioner that first suggests their use. One nurse noted that when patients return for subsequent visits, they sometimes mention picking up a probiotic “once the seed had been previously planted”.

Question 5: What kind of education or recommendations do you regularly provide to patients regarding side effects such as GI upset, diarrhea, yeast infection or other symptoms that they may experience with antibiotic use?

Explain or describe your usual practices regarding patient teaching.

All nine nurse practitioners had some patient education advice or materials regarding taking antibiotics that they shared with or provided to patients. Many educational materials focused on antibiotic effectiveness such as completing the antibiotic course, taking the antibiotic at the prescribed time or at the same time every day, and “connecting the antibiotic to another activity such as breakfast and dinner” so that it isn't forgotten. Less than half, 44% (n = 4) stated that they regularly address possible side effects of antibiotic use to their patients. Interviewee responses included taking medications with food to reduce stomach upset; three practitioners specifically stated what types of food to take with antibiotics, such as foods with a higher fat content. Three practitioners recommended increasing yogurt intake during the antibiotic treatment for cases that they considered at higher risk for side effects.

Questions 6: How do you feel about co-prescribing antifungal treatments such as Diflucan when you prescribe antibiotics?

All interviewees acknowledged that many patients with a history of yeast infection ask for Diflucan prescriptions. All except one practitioner, 88% (n = 8) stated that if a patient requests a prescription for Diflucan that they would provide it. Six of these interviewees (66%) were very clear that the patient has to request Diflucan, they never are first to bring up the topic. Two practitioners stated that if they see that Diflucan has been prescribed to that patient on a previous visit that they might ask the patient if they would like that again. Other interview comments included that denying a request for Diflucan was a barrier to care, and that patients

expect to receive it when they request it. One practitioner stated that not giving the prescription makes patients feel unheard or not respected and will encourage the patient to go to another provider or place for their care in the future. One practitioner expressed concern for comorbid conditions and medication interactions although this practitioner would not deny the request.

NPs offered patient education on the use of Diflucan. Patient education focused on waiting until the antibiotic is complete, 77% (n = 7), waiting until symptoms develop 77% (n = 7), and not taking the medication prophylactically 11% (n = 1). One NP recommended generating a “wait and see” prescription for Diflucan so the prescription is not available until after the antibiotic is finished. Finally, one respondent completely disagreed with the practice of prescribing Diflucan; this NP referred women to an over-the-counter yeast treatment product or recommended returning for professional diagnosis if symptoms persisted.

Discussion

All of the respondents had direct experience in the project subject matter of antibiotic-associated side effects. The average number of years in practice was 9.6 years, which indicates ample practice experience in prescribing medications and educating patients. Most nurse practitioners interviewed recognized a clinical value for probiotics for certain symptoms, patient populations, or scenarios.

A role for probiotics in the management of GI symptoms such as diarrhea was widely recognized by the healthcare providers. Although this indication strongly correlates with the evidence supporting probiotics for gastrointestinal symptoms including diarrhea and gastritis (Avadhani & Steefel, 2015; McFarland, 2015; World Gastroenterology, 2011) their knowledge of evidence-based recommendations for probiotic use did not correlate to the evidence. Several practitioners discussed the importance of maintaining balance of natural flora throughout the

body. This indication is also supported by literature (McFarland, 2015; World Gastroenterology, 2011). The NPs note certain scenarios when probiotics would be useful such as after colonoscopy, following viral illness, and with antibiotic use. Antibiotic use as an indication is well documented in the literature (Avadhani & Steefel, 2015; McFarland, 2015; Rodgers, et al., 2013; World Gastroenterology, 2011) the indications of post-colonoscopy and following viral illness are not specified in the literature, but GI literature was not a primary focus of this literature search. The nurse practitioners interviewed seemed to be considering causes of diarrhea and that is consistent with the literature. The NPs spoke of health literacy, populations likely to be receptive to probiotic use, and the inability of some patients to afford the supplements. The evidence selected did not address health literacy in respect to probiotic use, although the identification of middle-aged women years old did match with literature (Avadhani & Steefel, 2015), as well as the affordability of probiotic supplements (Avadhani & Steefel, 2015; McFarland, 2015). No practitioners discussed VVC in response to this question.

Nurse practitioners are well-experienced at prescribing antibiotics. Further, most of the NPs noted specific antibiotics or mentioned broad-spectrum antibiotics as likely to cause side effects for patients. Articles studied did list broad-spectrum antibiotics as a risk factor for antibiotic-associated side effects (Hanson, et al., 2016; Pirodda, et al., 2004). The NPs did pinpoint certain scenarios where probiotics would be helpful such as conditions needing higher doses of antibiotics (ear infections, animal bites), and cases where a second round of antibiotics was necessary. The literature did not specify causes that might be of higher risk for side-effect symptoms. The results from the interviews reveal that the nurse practitioners were aware of the findings from the literature based on their own experiences with patients.

Diarrhea or loose stools was a common symptom of concern voiced by the nurse practitioners interviewed. This side effect of antibiotic use is supported by the evidence of probiotic usefulness in cases of diarrhea (Avadhani & Steefel, 2015; McFarland, 2015; Rodgers, et al., 2013; World Gastroenterology, 2011). Yeast overgrowth was also voiced as a concern by the providers, specifically skin and oral thrush. These indications were supported by weaker evidence and this was not the primary focus in the search inclusion. Diabetes was mentioned by two NPs as a risk factor however, the literature did not identify this additional risk, nor was it a search inclusion for this project. The findings from the interviews suggest that side effects of antibiotic use are a concern of nurse practitioners however when suggesting probiotic use to combat these side effects their suggestions to patients may not be based on the best or current evidence.

Nurse practitioners interviewed rely on manufacturers packaging for guidance and information; advice not examined in any of the reviewed studies. One nurse practitioner stated that if package directions state one a day, but they are taking antibiotics, taking 2 or 3 each day of probiotic treatment would be recommended, this was consistent with research (Avadhani & Steefel, 2015; McFarland et.al, 2015). Only one interviewee recommended patients take the probiotic prior to antibiotic use. This advice was inconsistent with the evidence that is specific about separation doses by 2-4 hours (Avadhani & Steefel, 2015; Neafsey, 2005).

More than half of NPs recommended yogurt as a probiotic. Of these, two NPs stated “live active cultures”, one NP stated “Activa” – a name brand. The research was specific that not every yogurt is a probiotic (World Gastroenterology, 2011; McFarland et.al, 2015) and that live or active cultures are essential for yogurt to be an effective probiotic (World Gastroenterology, 2011; McFarland et.al, 2015) The brand name “Activa” was not noted in the

evidence although the brands “DanActive” was singled out as effective in one study (Hu, et al, 2013).

Surprisingly, all nine nurse practitioners stated that patients seldom ask about probiotics. Most NPs, replied that when probiotics are discussed it is most often the nurse practitioner that first suggests their use. There is no research data included that correlates to this research question. All nine nurse practitioners interviewees had some patient education advice or materials regarding taking antibiotics that they shared with or provided to patients. For most, the education had to do with completing the course, or taking with food; suggestions that were not researched or consistent with the objectives of this project. Specific foods were identified, a factor addressed only in one older study (Neafsey, 2005). Yogurt was recommended by three NPs, two mentioning live cultures in this question, a third just mentioning yogurt. The evidence suggests that to be considered a probiotic, a yogurt must contain, live, active cultures (World Gastroenterology, 2011; McFarland et.al, 2015).

All interviewees acknowledged that many patients with a history of yeast infection ask for Diflucan prescriptions. All except one practitioner would provide it. It should be noted that no articles were identified addressing this topic; Diflucan use was not the focus of this project.

Overall, nurse practitioners did not proactively address the known complication of VVC in susceptible patients unless the patient initiated the concern by requesting Diflucan. Interview questions regarding VVC were intentionally excluded to avoid leading responses. Interestingly, no nurse practitioners discussed the black box warning of Diflucan that was added in the past year recognizing a link between Diflucan and miscarriage (Davis Drug Guide, 2016). This was a concern to the author as the population most susceptible to VVC is women of childbearing age.

Conclusions

Although this quality improvement project initially focused on VVC, it became evident that while scientific evidence is stronger for use of probiotics with gastrointestinal symptoms; the evidence for use of probiotics for VVC symptoms is weak. While nurse practitioners are using probiotics clinically for symptoms consistent with research (i.e., GI symptoms), gaps in knowledge do exist that may prevent effective probiotic use. For example, if using probiotics for GI symptoms, if patients are not taught to space the antibiotic or probiotic products, then they may feel that the probiotics are ineffective without realizing that taking the products together has rendered the probiotic ineffective. Broad dissemination of current recommendations via an Executive Summary and in peer-reviewed journals for clinical practitioners may help to improve practice.

The source of probiotic information was an interesting finding in this project. All nurse practitioners stated that their formal education included no information on the use of probiotics. Common sources of information reported included product advertising, professional periodicals, and colleagues. Including some information on these products in pharmacology courses may help improve the ability of practitioners to best serve their patients.

Chapter Five: Implications to Practice

Practice Change Recommendations

While no significant practice changes were uncovered in this project, gaps in knowledge were identified that once remediated can improve patient medication compliance and enhance the clinician relationship in teaching patients how best to protect themselves and their families from discomforts related to antibiotic therapy. Publishing the recommendations in a professional journal for practitioners may help to improve practice by educating prescribers on the evidence-based recommendations that can improve treatment for their patients.

The evidence reveals that use of probiotics in the prevention or treatment of VVC is weak and does not support their use in clinical practice at this time. Evidence for probiotics for treatment of GI symptoms, both in the presence of antibiotics and in general is strong (Avadhani & Steefel, 2015; McFarland et.al, 2015; World Gastroenterology, 2011). Probiotic use in clinical practice must be based on human studies that support the intended health benefit. The research has uncovered these recommendations for optimal probiotic treatment:

- (a) Yogurts used as probiotics should contain live or active cultures, not every yogurt is considered a probiotic (World Gastroenterology, 2011; McFarland et.al, 2015).
- (b) 8-16 Ounces of yogurt with live cultures added provide similar health benefits as oral supplements (McFarland et.al, 2015).
- (c) Probiotic sources should contain 1-10 billion units of bacteria (McFarland et.al, 2015; World Gastroenterology, 2011).
- (d) Probiotics should be avoided in patients with high fevers or immunodeficiency (Avadhani & Steefel, 2015).

- (e) Avoid administering probiotics and antibiotics simultaneously as the antibiotic is likely to destroy the probiotic in the GI tract (Avadhani & Steefel, 2015; Neafsey, 2005; McFarland et.al, 2015).
- (f) When taking probiotics to prevent GI symptoms caused by antibiotics, the doses should be separated by two to four hours (Avadhani & Steefel, 2015; Neafsey, 2005).
- (g) When taking probiotics to prevent or treat antibiotic-associated GI symptoms, probiotics should be taken three to four times daily (Avadhani & Steefel, 2015).
- (h) When taking probiotics to replace flora disrupted by antibiotic therapy, the supplement should be continued for two weeks after the antibiotic treatment is finished (McFarland et.al, 2015).
- (i) Probiotic supplements should be taken in capsule form with an enteric coating to promote absorption in the small intestine and prevent destruction of the cultures by stomach acid (Avadhani & Steefel, 2015; Neafsey, 2005).
- (j) Read the package directions of any supplement before taking.

Limitations

The response rate for the interview snowball recruitment was nine out of nineteen, or 47%. According to Stommel and Wills (2004), response rates lower than 80% are associated with some level of bias. The NPs invited received a recruitment letter that introduced the focus of the project. It is possible that NPs that did not feel comfortable discussing their knowledge or professional practices declined the invitation while practitioners who were more knowledgeable or confident chose to participate. This selective option may have contributed to bias.

A PNP was included in the participants. PNPs do not treat the age group selected for the project and thus may have contributed to bias for GI symptoms. The age range selected for this

project was 21 to 45 years of age. The age of 18 is the age of consent and if repeated, women between the ages of 18 and 45 should be included.

The open-ended question format, and the goal of limiting the interview to six questions may have inadvertently limited the findings. Although interesting findings were uncovered, more detailed questioning may have produced more detailed responses. Repeating the project with questions regarding VVC, effective organisms, and a broader recruitment method would likely produce more specific and useful results.

Implications for Nursing Practice and the Doctor of Nursing Practice Essentials

The DNP Essentials of Doctoral Education for Advanced Practice Nurses (American Association of Colleges of Nursing, 2006) and their relevance to this project include:

Essential I: Scientific underpinnings for practice.

Scientific underpinnings include nursing theories, models, and philosophies. In this project, the theoretical framework of PARIHS, designed as a guide to implement EBP in clinical practice was used. The Iowa model was applied to navigate the intricacies of change. Finally, the literature evaluation and synthesis of the evidence-based literature are the foundation providing the scientific underpinnings of advanced practice nursing.

Essential II: Organizational and systems leadership for quality improvement and systems thinking.

Systems leadership encompasses the facilitation of multiple interacting and intersecting systems to affect change. This essential was represented through navigation of the corporate environment, the college environment, and the project plan. All parties were not in agreement on the goals and definition of the project requiring organizational and systems leadership to

navigate a path to successful project completion including an executive summary of evidence-based practice recommendations.

Essential III: Clinical scholarship and analytical methods for evidence-based practice.

This essential is represented in the DNP project in identifying the problem, performing a methodical literature review, analysis of evidence-based literature, and translation of findings into clinical practice recommendations. Analytic methods to interpret the data allowed the identification of studies and articles of highest statistical worth.

Essential IV: Information systems/technology and patient care technology for the improvement and transformation of healthcare.

This essential was represented through the comprehensive literature search. *Melnyk's Center for Transdisciplinary Evidence Based Practice Rapid Critical Appraisal Tool* (2011) was utilized to analyze and identify data of highest statistical worth. These skills are instrumental in obtaining appropriate and accurate health information evidence on which to base change.

Essential V: Healthcare policy for advocacy in health care. Remediation of patient teaching points and dissemination of findings should lead to policy change at the clinic level so that practice is current with evidence.

Essential VI: Inter-professional collaboration for improving patient population.

Assuming leadership roles and employing effective communication skills were essential to the project's successful completion.

Essential VII: Clinical prevention and population health for improving the nation's health.

This essential is at the core of this DNP project. Probiotics as a prevention to improve the patient experience and improve medication compliance with antibiotics does contribute to the nation's health. This project employing health promotion and risk reduction improves the patient's treatment experience.

Essential VIII: Advanced nursing practice.

This project sought to identify what NPs taught their patient and compared this to current evidence identifying what exactly we should be teaching patients about probiotics when an antibiotic is prescribed. Nurse practitioners are well known for patient-centered education and holistic a view of the patient. The results of this project clarify evidence-based recommendations for probiotic use, improving patient experiences and advancing nursing practice.

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Appendix A

EBP Synthesis Table

Author / Study	LOE / Design	Year	Pertinent Sample Characteristics	Specific Probiotic	Intervention	Major findings r/t PICOT
Abad & Safdar The role of Lactobacillus Probiotics in the Treatment of Prevention of Urogenital Infections – A Systematic Review	I Systematic Review	2009	Examined 25 studies to evaluate effectiveness of probiotic on development of BV, UTI, and VVC	Lactobacillus	Women with recurrent infections, not necessarily related to ABX use. Probiotic compared to no treatment	Significant benefit for BV. Evidence for prevention in UTI or VVC was “uncertain”
Bohbot, J. M., & Cardot, J. M. Vaginal impact of the Oral Administration of Total Freeze-Dried Culture of LCR 35 in Healthy Women	II Randomized RCT	2011	20 women childbearing age in Paris 10 Women in each group ages 18-45 years old, premenopausal, non-pregnant with effective contraception, non-immunodeficient, no anti-infectious tx.	Lactobacillus casei rhamnosus (LCR 55)	effectiveness of 2 doses LCR35	vaginal uptake of different doses may demonstrate greater use of probiotics as prophylactic tx Both groups positive effect, higher dose had better outcome Positive relationship between oral and vaginal uptake Further research is necessary to specify preventative or curative impact
Hanson, et al. Probiotics for Treatment and prevention of Urogenital Infections in Women: A systematic Review	I Systematic Review	2008-2015	20 Studies Reviewed		Of 20 studies, 2 focused on VVC	“Variable findings” Results did not indicate usefulness in prevention or treatment, but ongoing use of probiotic can help prevent recurrence

Hu, et al. Impact of Eating Probiotic Yogurt on Colonization by Candida Species of the Oral and Vaginal mucosa in HIV-infected and HIV-uninfected women	III Pilot study as part of an ongoing longitudinal study	2013	24 Women (17 HIV+, 7 HIV-), Georgetown University. Exclusion: women w/hysterectomies, trying to conceive, or tx w/any antifungal during study period. some women were HIV+ thus likely immune-compromised	2 Branded products represented the two major genera Less fungal colonization in all groups consuming probiotic yogurt 54% none probiotic period, 29% w/DanActive, 38% w/YoPlus	The Women went 60 days without yogurt, then DanActive (one 3.1 oz container per day) for 15 days, followed by a 30-day wash out period, and finally a 15 days course of YoPlus (one 4oz container per day) yogurt. Oral and vaginal samples were obtained at each completion point, 4 in all	addresses probiotic in yogurt form Addressed treatment and prevention Less fungal colonization in all groups consuming probiotic yogurt 54% none probiotic period, 29% w/DanActive, 38% w/YoPlus significant difference between the two yogurt types “No statistically significant differences were found between treatment periods, and non-treatment periods”
McFarland, L From Yaks to Yogurt: The History, Development, and Current Use of Probiotics	VII Article/Expert Opinion	2015		Acidophilus, Lactobacillus	Patient beliefs, marketing, evidence-based efficiency indications	VVC not well studied (6% of research) Evidence of other uses for probiotics
Neafsey, P Bugs, Drugs, and Yogurt	VII Expert opinion	2005	Review of studies in early 2005, admits that studies do not meet EBP criteria but do show positive correlation w/Lactobacillus	Lactobacilli	Specific recommendations regarding dosing, and how to administer as preventative measure	Specifically supportive of PICOT
Pendharkar, et al. Vaginal colonization by probiotic lactobacilli can clinical outcome in women conventionally treated for bacterial vaginosis and yeast infection	III 2 consecutive open-label pilots	2011	40 Scandinavian women w/ BV, VVC, or clinical symptoms. > 18 years old, non pregnant, no signs of other GU infection.	Dual probiotic containing Lactobacillus rhamnosis & Lactobacillus gasseri Labeled as EcoVag	#1: BV only tx w/ clindamycin & metronidazole followed by EcoVag 5 days after each atb tx. 2: BV and Yeast: divided to 3 groups: a) BV receiving clindamycin and metronidazole w/ EcoVag for 10 days after each atb tx then weekly tx for 4 months. b) R-VVC receiving extended fluconazole and EvoVag tx c) extended fluconazole tx only d)	Product contains 2 strains Lactobacillus Treatment effective for BV, further studies needed for VVC

Pirotta, et al. The PAV trial: Does lactobacillus prevent post-antibiotic vulvovaginal candidiasis? A randomized controlled trial	II Randomized, placebo controlled, double blind, factorial 2x2 trial	2004	235 Women 18-50 years old, starting a short term atb for non-uro/gyn acute infection 50 general practices & 16 pharmacies in Melbourne Australia	Lactobacillus	Compare oral VS vaginal administration of probiotic	largest quality study to investigate the effects of probiotic use in prevention of VVC Treatment was deemed ineffective Study stopped early due to result results in opposition to common practice
Pirotta & Garland Her Choice: Dealing with Lactobacilli, Vaginitis, and Antibiotics	VII Expert Opinon by researcher of PAV trial	2005		Lactobacillus	Discusses historic acceptance in medical community and ages old patient belief. Believes that most VVC is not accurately diagnosed (is self diagnosed by patients)	“Despite being a popular folk remedy with decades of acceptance and use evidence is weak.”
Reid & Bruce Urogenital infections in women: can probiotics help	VII Article/Expert opinion	2003	Discussion of pathophysiology, organisms, many references to existing studies, but not a systematic review	Several	N/A – discussion	No scientific evidence of antifungal activity.
Vicariotto, et al. Effectiveness of the association of 2 probiotic strains formulated in a slow release vaginal product, in women affected by vulvovaginal candidiasis; a pilot study	III Pilot Study	2012	30 Women diagnosed with VVC, prone to recurrence.	Dual probiotic agent containing Lactobacillus fermentum LF10 & Lactobacillus acidophilus	All received intervention Results compared to previous study recurrence points. Intravaginal product	Nearly all had success in 1st month. All but three avoided recurrence in 2nd month. Dual probiotic with success “effectiveness in acute VVC infection, but does not offer long term protection in recurrence”

Legend: LOE=Level of evidence, VVC=Vulvovaginal candidiasis, BV=Bacterial Vaginosis, Tx=treatment

Appendix B

The Ohio State University-College of Nursing	
Human Subjects Research Assessment Form	
Instructions:	
1. Please complete the requested project information, as this form may be used for documentation that neither IRB review nor an exemption is required. 2. Please select the appropriate answers to each question in order as they appear. If all of the questions are answered without receiving an error message, the form must be printed AND signed as certification that the project is "not human subjects research," and does not require IRB review or exemption. If you are unsure how to answer any of the questions, please contact ORRP for additional guidance.	
Project Information:	
Name of PI, advisor, or mentor:	Laureen Smith
Title of Project	Beliefs and practices of NPs related to the use and recommendation of probiotics for prevention of antibiotic associated VVC
Brief Description of Project/Goals:	This quality improvement project aims to compare current practice to current evidence regarding clinical recommendation of probiotics to provide a practice change recommendation if warranted. The project will use an interview format to gather responses from nurse practitioners who prescribe antibiotics regarding their beliefs and practices of including or recommending probiotics to prevent or relieve antibiotic associated side effects. A comprehensive review and analysis of current literature will be compared to the responses to inform treatment and patient education practices to better act in accordance with current evidence.
	Help
Questions:	
1. Will the project involve testing an experimental drug, device (including medical software or assays), or biologic? <input type="radio"/> Yes <input checked="" type="radio"/> No	Help
2. Has the project received funding (e.g. federal, industry) to be conducted as a human subjects research study? <input type="radio"/> Yes <input checked="" type="radio"/> No	Help
3. In addition to any other purposes, is the project intended to develop or contribute to <u>generalizable knowledge</u> (e.g. testing a hypothesis) AND/OR has the project been designed in such a way that the findings will be generalizable (e.g. randomization of subjects; comparison of case vs. control)? <input type="radio"/> Yes <input checked="" type="radio"/> No	Help
4. Will the results of the project be published, presented or disseminated outside of the institution conducting it? <input checked="" type="radio"/> Yes <input type="radio"/> No	Help
5. Will the project occur exactly as proposed regardless of whether individuals conducting it may benefit professionally from it? <input checked="" type="radio"/> Yes <input type="radio"/> No	Help
6. Is the project intended to improve or evaluate the practice or process within a particular institution or a specific program? <input checked="" type="radio"/> Yes <input type="radio"/> No	Help
If no message appears above indicating the certification is not valid, IRB Review is not required because, in accordance with federal regulations, the project does not constitute human subjects research as defined under 45 CFR 46.102(d). Print a copy of this form, have it signed by the PI, advisor, or mentor, and save with your files. This serves as record that IRB review is not required for this project.	
What do my results mean?	Signature: <u>Laureen H. Smith</u> 9-6-16
Current Date: 9/5/16	Print Form

Appendix C

DISCLOSURE AND CONSENT FORM

Project Title: Beliefs and Practices of Nurse Practitioners Related to the Use and Recommendation of Probiotics in the Prevention or Treatment of Antibiotic-Associated Side Effects.

You are being invited to participate in a quality-improvement project being conducted by Donnamarie Burris, a Doctor of Nursing Practice student enrolled at the Ohio State University. Please review this form prior to your participation so that you are aware of potential risks and how the information you provide will be used. If you decide to take part in the project, your responses will be anonymous.

The purpose of the project is to evaluate the beliefs and practices of nurse practitioners regarding the use or recommendation of probiotic products. Survey results will be compared to current evidence to describe and analyze best practices of uses for probiotics in the clinical setting. The results from these interviews may help other nurse practitioners in augmenting their practice recommendations in the clinical uses and effectiveness of probiotics as adjunctive treatment.

The interview will be conducted in-person in a private and confidential location at the convenience of the participant. The interview will last approximately ten to fifteen minutes. The interviewer will make handwritten notes on the interview form, and the interview will be recorded without including information about the participant or other identifying information. The recording will be destroyed after it has been transcribed and confirmed to be accurate.

The interview will consist of six questions, plus follow up questions if appropriate. Optional demographic information will be collected. Although the questions have been structured to avoid risks, you do not have to answer any questions that you do not want to answer. If you decide to quit at any time prior to completing the survey, your answers will not be recorded. There may be no direct benefit to you by participating in the project.

Information about you will be kept confidential to the extent permitted or required by law. After data collection is completed, all participant contact information will be destroyed. If there are any professional presentations or publications about this study or survey responses, your name, practice name, e-mail address, or postal address will not be included.

By beginning the interview, you acknowledge that you have read this information and agree to participate in this research survey, with the knowledge that you are free to withdraw your participation at any time without penalty.

Appendix D

Interview Questions

1. What are your thoughts and experiences regarding the clinical recommendation of probiotics for patients?
2. Do you prescribe antibiotics? If so, what is your experience with the efficacy of probiotics to prevent or treat antibiotic-associated side effects?
 - 2a. What symptoms are you concerned about?
 - 2b. I do not recommend probiotics to my patients who are taking antibiotics.
3. If you recommend probiotics to patients, how do you recommend they be taken?
 - 3a. If you do not recommend them, can you tell me why you do not?
4. Do patients ask about probiotic use when you prescribe antibiotics?
Describe or explain how you respond.
5. What kind of education or recommendations do you regularly provide to patients regarding side effects such as GI upset, diarrhea, yeast infection or other symptoms that they may experience with antibiotic use?

Explain or describe your usual practices regarding patient teaching.
6. How do you feel about co-prescribing antifungal treatments such as Diflucan when you prescribe antibiotics?

Appendix E

INVITATION TO PARTICIPATE
IN A DOCTORATE OF NURSING PRACTICE (DNP) PROJECT
REGARDING PROBIOTICS

You are being invited to participate in a quality-improvement project being conducted by Donnamarie Burris, a Doctor of Nursing Practice student enrolled at the Ohio State University. The purpose of the project is to evaluate the beliefs and practices of nurse practitioners regarding the use or recommendation of probiotic products. The results from this project may help other nurse practitioners in augmenting their practice recommendations in the clinical uses and effectiveness of probiotics as adjunctive treatment.

Your participation in the project will be voluntary and anonymous. The interview will be conducted in-person in a private and confidential location at your convenience. The interview will last approximately ten minutes. The interview will consist of six questions, plus follow up questions if appropriate. Optional demographic information will be collected. Although the questions have been structured to avoid risks, you do not have to answer any questions that you do not want to answer. If you decide to quit at any time prior to completing the survey, your answers will not be recorded.

Thank you for your consideration and contribution to the future of our profession. I know your time is valuable and I am grateful for the opportunity to include your input in my findings. If you are willing to participate, please contact me, the student, by either phone or email listed below.

Sincerely,

Donnamarie Burris
(602) 363-3108
DonnamarieBurris@gmail.com

Appendix F

Beliefs and Practices of Nurse Practitioners Related to the Use and Recommendations of Probiotics for the Prevention of Antibiotic-Associated Vulvovaginal Candidiasis in Adult-aged Women: An Opportunity for Evidence-based Practice Change.

EXECUTIVE SUMMARY

Donnamarie Burris, MSN, RN, CNP

Subject Matter / Purpose

The purpose of this quality improvement project was twofold:

- (a) Conduct semi-structured interviews to explore the beliefs and current practices of Nurse Practitioners (NPs) that prescribe antibiotic therapy in the outpatient setting, regarding probiotic products
- (b) Compare these beliefs and practices to the best current evidence. A synthesis of the literature was conducted to describe and critically analyze current best practices of probiotic use in the clinical setting.

Methods of Analysis

The project design included qualitative semi-structured interviews of nine NPs identified using a snowball recruitment method. Responses were recorded on an interview form and common themes to each question were analyzed. Responses were compared to current evidence-based literature from sixteen peer-reviewed articles that examined the effectiveness of probiotics in the prevention or treatment of certain antibiotic associated side effects.

Findings

Although the practitioners' beliefs of symptoms to address with probiotics were generally consistent with current best evidence, gaps in knowledge were identified. The recommendation of probiotic strains and the number of cultures contained in the supplement were discussed in some interviews but was not always in agreement with the literature. Similarly, suggestions regarding the frequency and timing of dosing between the probiotic and the antibiotic voiced by the practitioners were often inconsistent with the research findings.

Conclusions

Although this quality improvement project initially focused on VVC, it became evident that while scientific evidence is stronger for use of probiotics with gastrointestinal symptoms; the evidence for use of probiotics for VVC symptoms is weak. While nurse practitioners are using probiotics clinically for symptoms consistent with research (i.e., GI symptoms), gaps in knowledge do exist that may prevent effective probiotic use. For example, if using probiotics for GI symptoms and patients are not taught to space the antibiotic or probiotic products, then they may feel that the probiotics are ineffective without realizing that taking the products together has rendered the probiotic ineffective. Broad dissemination of current recommendations via an Executive Summary and in peer-reviewed journals for clinical practitioners may help to improve practice.

The source of probiotic information was an interesting finding in this project. All nurse practitioners stated that their formal education included no information on the use of probiotics. Common sources of information reported included product advertising, professional periodicals, and colleagues. Including some information on these products in pharmacology courses may help improve the ability of practitioners to best serve their patients. The results from the semi-structured interviews may augment practice recommendations in clinic settings and effectiveness of probiotics as adjunctive treatment.

Recommendations

The main recommendation for the use of probiotics is to suggest probiotics when antibiotics are prescribed to prevent or treat antibiotic-associated diarrhea. Current evidence suggests that probiotics are not effective to prevent or treat vulvovaginal candidiasis. The research has uncovered these recommendations for optimal probiotic treatment:

- (k) Yogurts used as probiotics should contain live or active cultures.
- (l) 8-16 Ounces of yogurt with live cultures added provide similar health benefits as oral supplements.
- (m) Probiotic sources should contain 1-10 billion units of bacteria.
- (n) Probiotics should be avoided in patients with high fevers or immunodeficiency.
- (o) Avoid administering probiotics and antibiotics simultaneously as the antibiotic is likely to destroy the probiotic in the GI tract.
- (p) When taking probiotics to prevent GI symptoms caused by antibiotics, the doses should be separated by two to four hours.
- (q) When taking probiotics to prevent or treat antibiotic-associated GI symptoms, probiotics should be taken three to four times daily.
- (r) When taking probiotics to replace flora disrupted by antibiotic therapy, the supplement should be continued for two weeks after the antibiotic treatment is finished.
- (s) Probiotic supplements should be taken in capsule form with an enteric coating to promote absorption in the small intestine and prevent destruction of the cultures by stomach acid.
- (j) Read the package directions of any supplement before taking.

Limitations of the Report

The response rate for the interview snowball recruitment was 47%, response rates lower than 80% may be associated with some level of bias. The NPs invited received a recruitment letter that introduced the focus of the project. It is possible that NPs that did not feel comfortable discussing their knowledge or professional practices declined the invitation while practitioners who were more knowledgeable or confident chose to participate. This selective option may have contributed to bias.

The open-ended question format, and the goal of limiting the interview to six questions may have inadvertently limited the findings. Although interesting findings were uncovered, more detailed questioning may have produced more detailed responses. Repeating the project with questions regarding VVC, effective organisms, and a broader recruitment method would likely produce more specific and useful results.